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CLAIMS

What is claimed is:

- A method of inhibiting fibrosis in a patient said method comprising administering a therapeutically effective amount of somatostatin or a somatostatin agonist to said patient.
- 2. A method of claim 1, wherein said method comprises administering a therapeutically effective amount of a somatostatin agonist to said patient.
 - 3. A method of claim 2, wherein said fibrosis is in the kidney.
 - 4. A method of claim 2, wherein said fibrosis is in the lung.
- 15 5. A method of claim 2, wherein said fibrosis is in the liver.
 - 6. A method of claim 2, wherein said fibrosis is in the skin.
- 7. A method of claim 2, wherein said fibrosis is induced by chemotherapy.
 - 8. A method of claim 2 wherein said somatostatin agonist is administered parenterally.
 - 9. A method of cam 8, wherein said somatostatin agonist is administered in a sustained release formulation.
- 25 10. A method of claim 3 wherein said somatostatin agonist is administered parenterally.
 - 11. A method of claim 10, wherein said somatostatin agonist is administered in a sustained release formulation.
 - 12. A method of claim 4, wherein said somatostatin of agonist is administered parenterally.
 - 13. A method of claim 12, wherein said somatostatin agonist is administered in a sustained release formulation.
 - 14. A method of claim 5, wherein said somatostatin agonist is administered parenterally.



16. A method of claim 14, wherein said somatostatin agonist is administered in a sustained release formulation.

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- 16. A method of claim 6, wherein said somatostatin agonist is administered parenterally.
- 17. A method of claim 2, wherein said somatostatin agonist is administered topically.
- 18. A method of claim 7, wherein said somatostatin agonist is administered parenterally.
- 19. A method of claim 18, wherein said somatostatin
 10 agonist is administered in a sustained release formulation.
 - 20. A method according to claim 2 wherein the fibrosis is induced by radiation.
 - 21. A method according to claim 3 wherein the fibrotic disorder in the kidney is glomerulonephritis.
- 22. A method according to claim 3 wherein the fibrotic disorder in the kidney is diabetic nephropathy.
 - 23. A method according to claim 3 wherein the fibrotic disorder in the kidney is allograft rejection.
- 24. A method according to claim 3 wherein the fibrotic disorder in the kidney is AIV nephropathy.
 - 25. A method according to claim 4 wherein the fibrotic disorder in the lung is idippathic fibrosis.
 - 26. A method according to claim 4 wherein the fibrotic disorder in the lung is autoimmine fibrosis.
- 25 27. A method according to claim 5 wherein the fibrotic disorder in the liver is cirrhosis.
 - 28. A method according to claim 5 wherein the fibrotic disorder in the liver is veno-occlusive disease.
- 29. A method according to claim 6 wherein the fibrotic 30 disorder in the skin is systemic sclerosis.
 - 30. A method according to claim 6 wherein the fibrotic disorder in the skin is keloids.
 - 31. A method according to claim 6 wherein the fibrotic disorder in the skin is scars.



- 32. A method according to claim 6 wherein the fibrotic disorder in the skin is eosinophilia-myalgia syndrome.
- 33. A method according to claim 2 wherein the fibrosis is of the central nervous system.
- 34. A method according to claim 33 wherein the fibrotic disorder is intraocular fibrosis.
 - 35. A method according to claim 2 wherein the fibrosis is in bone or bone marrow.
- 36. A method according to claim 2 wherein the fibrosis 10 is in the cardiovascular system.
 - 37. A method according to claim 2 wherein the fibrosis is in an endocrine organ.
 - 38. A method according to claim 2 wherein the fibrosis is in the gastrointestinal system.
- 39. A method according to claim 7 wherein the fibrosis induced by chemotherapy is induced by chemotherapy is induced by chemotherapy.
 - 40. A method according to claim 7 wherein the fibrosis induced by chemotherapy is it, the lung.
- 41. A method according to claim 7 wherein the fibrosis 20 induced by the chemotherapy As in the liver.
 - 42. A method according to claim 7 wherein the fibrosis induced by the chemotherapy is in the skin.
 - 43. A method according to claim 7 wherein the fibrosis induced by the chemotherapy is of the central nervous system.
- 25 44. A method according to claim 7 wherein the fibrosis induced by the chemotherapy is in hone or bone marrow.
 - 45. A method according to claim 7 wherein the fibrosis induced by the chemotherapy is in the cardiovascular system.
- 46. A method according to claim 7 wherein the fibrosis induced by the chemotherapy is in an endocrine organ.
 - 47. A method according to claim 7 wherein the fibrosis induced by the chemotherapy is in the gastrointestinal system.



20

48. A method according to claim 20 wherein the fibrosis induced by radiation is in the kidney.

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- A method according to claim 20 wherein the fibrosis induced by radiation is in the lung.
- A method according to claim 20 wherein the fibrosis induced by the radiation is in the liver.
- 51. A Method according to claim 20 wherein the fibrosis induced by the radiation is in the skin.
- 52. A medhod according to claim 20 wherein the fibrosis induced by the Adiation is of the central nervous system. 10
 - 53. A metho ϕ according to claim 20 wherein the fibrosis induced by the radiation is in bone or bone marrow.
 - 54. A method according to claim 20 wherein the fibrosis induced by the radiation is in the cardiovascular system.
- 1.5 55. A method acording to claim 20 wherein the fibrosis induced by the radiation is in an endocrine organ.
 - 56. A method according ψg claim 20 wherein the fibrosis induced by the radiation is if the gastrointestinal system.
 - 57. A method $acc\phi rdihg/to claim 2$ wherein the fibrosis is induced by a drug or a combination of drugs.
 - 58. A method acdording to claim 2 wherein the fibrosis is induced by a disease state
 - 59. A method according t > 0 claim 2 wherein the fibrosis is induced by an environmental or an industrial factor.
- 60. A method according to ${}^{\ }$ laim 2 wherein the fibrosis 25 is induced by an immune reaction.
 - 61. A method of inhibiting of erexpression of TGF- β which comprises administering to a Aubject an effective amount of somatostatin, somatostatin agonist or a pharmaceutically acceptable salt thereof.
 - 62. A method according to claim 61 wherein a somatostatin agonist is administered.
 - 63. A method according to claim 62\wherein the



omatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 1 than the other human somatostatin sub-type receptors.

- 64. A method according to claim 62 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 2 than the other human somatostatin sub-type receptors.
- 65. A\method according to claim 62 wherein the somatostatin\agonist has a higher binding affinity for human somatostatin sub-type receptor 3 than the other human somatostatin sub-type receptors.
 - 66. A meth λ d according to claim 62 wherein the somatostatin agon \mathbf{i}_{ξ} t has a higher binding affinity for human somatostatin sub-type receptor 4 than the other human somatostatin sub-type receptors.
 - 67. A method according to claim 62 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 5 than the other human somatostatin sub-type/recemptors.
- 68. A method according to claim 62 wherein the 20 somatostatin agonist has h higher binding affinity for two or more of human somatostatin redeptor sub-types 1, 2, 3, 4 and/or 5.
- 69. A method according to tlaim 62 wherein the 25 somatostatin agonist is

$$R_1$$

$$A^1-A^2-A^3-D-Trp-Lys-A^6-A^7-A^8-R_1$$

$$R_2$$

or a pharmaceutically acceptable salt thereof, wherein

A¹ is a D- or L- isomer of Ala, L\u03c6u, Ile, Val, Nle,

Thr, Ser, β -Nal, β -Pal, Trp, Phe, 2,4-dich oro-Phe, 35 pentafluoro-Phe, p-X-Phe, or o-X-Phe;

30

 A^2 is Ala, Leu, Ile, Val, Nle, Phe, β -Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe;

A³ is pyridyl-Ala, Trp, Phe, β-Nal, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe;

 A^6 is Val, Ala, Leu, Ile, Nle, Thr, Abu, or Ser; A^7 is Ala, Leu, Ile, Val, Nle, Phe, β -Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe;

10 $A^8 \text{ is a D-or L-isomer of Ala, Leu, Ile, Val, Nle,} \\ \text{Thr, Ser, Phe, } \beta\text{-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe,} \\ \text{pentafluoro-Phe, p-X-Phe, or o-X-Phe;} \\ \text{wherein X for each occurrence is independently selected from the group consisting of CHz, Ol, Br, F, OH, OCH3 and NO2;} \\$

each R_1 and R_2 , independently, is H, lower acyl or lower alkyl; and R_3 is OH of NH_2 ; provided that at least one of A^1 and A^8 and one of A^2 and A^7 must be an aromatic amino acid; and further provided that A^1 , A^2 , A^7 and A^8 cannot all be aromatic amino acids.

70. A method according to claim 62 wherein the somatostatin agonist is

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Thr-Phe-Thr-NH₂;

H-D-Phe-p-NO₂-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

H-D-Nal-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

H-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH₂;

H-D-Phe-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂; or

H-D-Phe-Ala-Tyr-D-Trp-Lys-Val-Ala-β-D-Nal-NH₂ or a pharmaceutically acceptable salt thereof.

71. A method according to claim 62 wherein the somatostatin agonist is D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys- β -Nal-NH;

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          -Cys-Tyr-D-Trp-Lys-Thr-Cys-\beta-Nal-NH<sub>2</sub>;
    D-β-N&1-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH<sub>2</sub>;
    D-Phe-dys-Tyr-D-Trp-Lys-Thr-Pen-Thr-NH2;
    D-Phe-C\s-Phe-D-Trp-Lys-Thr-Pen-Thr-NH2;
    D-Phe-Cy&-Tyr-D-Trp-Lys-Thr-Pen-Thr-OH;
    D-Phe-Cys \Phe-D-Trp-Lys-Thr-Pen-Thr-OH;
     Gly-Pen-Pha-D-Trp-Lys-Thr-Cys-Thr-OH;
     Phe-Pen-Tyr-D-Trp-Lys-Thr-Cys-Thr-OH;
     Phe-Pen-Phe-D-Trp-Lys-Thr-Pen-Thr-OH;
    H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-ol;
10
     H-D-Phe-Cys-Phe D-Trp-Lys-Thr-Cys-Thr-NH2;
     H-D-Trp-Cys-Tyr-V-Trp-Lys-Val-Cys-Thr-NH2;
     H-D-Trp-Cys-Phe-D\Trp-Lys-Thr-Cys-Thr-NH2;
     H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH2;
     H-D-Phe-Cys-Tyr-D-Tap-Lys-Val-Cys-Trp-NH2;
15
     H-D-Phe-Cys-Tyr-D-Tr\(\frac{1}{2}\)-Lys-Val-Cys-Thr-NH2;
     Ac-D-Phe-Lys -Tyr-D-Trp-Lys-Val-Asp-Thr-NH2, wherein an amide
     bridge is between Lys
                               and Asp;
     Ac-hArg(Et)2-Gly-Cys-Ph D/frp-Lys-Thr-Cys-Thr-NH2;
     Ac-D-hArg(Et)2-Gly-Cys/Phe-Trp-Lys-Thr-Cys-Thr-NH2;
20
     Ac-D-hArg(Bu)-Gly-Cys-Phe-M-Trp-Lys-Thr-Cys-Thr-NH2;
     Ac-D-hArg(Et) 2-Cys-Phe D-Trh-Lys-Thr-Cys-Thr-NH2;
     Ac-L-hArg(Et)<sub>2</sub>-Cys-Phe-D-Trb\Lys-Thr-Cys-Thr-NH<sub>2</sub>;
     Ac-D-hArg(CH<sub>2</sub>CF<sub>3</sub>)<sub>2</sub>-Cys-Phe-D-T-T-Lys-Thr-Cys-Thr-NH<sub>2</sub>;
     Ac-D-hArg(CH2CF3)2-Gly-Cys-Phe-\(\frac{1}{2}\)-Trp-Lys-Thr-Cys-Thr-NH2;
25
    Ac-D-hArg(CH2CF3)2-Gly-Cys-Phe-D\Trp-Lys-Thr-Cys-Phe-NH2;
     Ac-D-hArg(CH2CF3)2-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;
     Ac-L-hArg(CH2-CF3)2-Gly-Cys-Phe-D-trp-Lys-Thr-Cys-Thr-NH2;
     Ac-D-hArg(CH<sub>2</sub>CF<sub>3</sub>)<sub>2</sub>-Gly-Cys-Phe-D-TrA-Lys(Me)-Thr-Cys-Thr-NH<sub>2</sub>;
     Ac-D-hArg(CH<sub>2</sub>CF<sub>3</sub>)<sub>2</sub>-Gly-Cys-Phe-D-Trp\Lys(Me)-Thr-Cys-Thr-NHEt;
30
     Ac-hArg(CH3, hexyl)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH2;
      H-hArg(hexyl2)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH2;
      Ac-D-hArg(Et)<sub>2</sub>-Gly-Cys-Phe-D-Trp-Lys-Th\(\alpha\)-Cys-Thr-NHEt;
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cvclo (N-Me-Ala-Tyr-D-Trp-Lys-Thr-Phe);
   cyclo (Pro-Tyr-D-Trp-Lys-Thr-Phe);
   cyclo (Pro-Phe-D-Trp-Lys-Thr-Phe);
   cyclo (Pro-Phe-L-Trp-Lys-Thr-Phe);
  cyclo \Pro-Phe-D-Trp(F)-Lys-Thr-Phe);
    cyclo (Pro-Phe-Trp(F)-Lys-Thr-Phe);
    cyclo (Pko-Phe-D-Trp-Lys-Ser-Phe);
    cyclo (Pr&-Phe-D-Trp-Lys-Thr-p-Cl-Phe);
    cyclo (D-A Na-N-Me-D-Phe-D-Thr-D-Lys-Trp-D-Phe);
    cyclo (D-Ala-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Phe);
10
    cyclo (D-Ala-W-Me-D-Phe-D-Thr-Lys-D-Trp-D-Phe);
    cyclo (D-Abu-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Tyr);
    cyclo (Pro-Tyr-\p-Trp-t-4-AchxAla-Thr-Phe);
    cyclo (Pro-Phe-D\Trp-t-4-AchxAla-Thr-Phe);
    cyclo (N-Me-Ala-T)\r-D-Trp=Lys-Val-Phe);
15
    cyclo (N-Me-Ala-Ty) -D-/rp-/-4-AchxAla-Thr-Phe);
                         (4-Amone-Thr-Phe);
     cyclo (Pro-Tyr-D-Trp
    cyclo (Pro-Phe-D-Trp-V-Amphe-Thr-Phe);
     cyclo (N-Me-Ala-Tyf-D-Mrp-4-Amphe-Thr-Phe);
     cyclo (Asn-Phe-Phe-D-T/rA-Lys-Thr-Phe-Gaba);
20
     cyclo (Asn-Phe-Phe-Phe-Gaba-Gaba);
     cyclo (Asn-Phe-D-Trp-Lys-Thr-Phe);
     cyclo (Asn-Phe-Phe-D-Trp-Ly&-Thr-Phe-NH(CH2)4CO);
     cyclo (Asn-Phe-Phe-D-Trp-Lys\Thr-Phe-\beta-Ala);
     cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-D-Glu) -OH;
     cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe);
     cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe+Gly);
     cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
     cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gly);
 30 cyclo (Asn-Phe-Phe-D-Trp(F)-Lys-Thr\Phe-Gaba);
     cyclo (Asn-Phe-Phe-D-Trp(NO2)-Lys-Thr Phe-Gaba);
     cyclo (Asn-Phe-Phe-Trp(Br)-Lys-Thr-Pha-Gaba);
     cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe(I)-Gaba);
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cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Tyr(But)-Gaba);

cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-OH;

cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-OH;

cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-MeLeu-Cys)-OH;

cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-MeLeu-Cys)-OH;

cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Phe-Gaba);

cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Phe-Gaba);

cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Phe-Gaba);

cyclo (Asn-Phe-Phe-D-Trp-Lys(Ac)-Thr-Phe-NH-(CH<sub>2</sub>)<sub>3</sub>-CO);

cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);

cyclo (Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);

cyclo (Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);

cyclo (Orn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba) or a

pharmaceutically acceptable salt thereof.

72. A method according to claim 62 wherein the
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- 72. A method according to claim 62 wherein the somatostatin agonist is $D-\beta$ -Nal-Cys-Tyr-D-Trp-Lys-Thr-Cys-Thr-NH₂ or a pharmaceutically acceptable salt thereof.
- 73. A method according to claim 62 wherein the somatostatin agonist is H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH2 or a pharmaceutically acceptable salt thereof.
 - 74. A method according to claim 62 wherein the somatostatin agonist is

$$HO(CH_2)_2 - N$$
 $N - (CH_2)_2 - SO_2 - D - Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH2,$

or a pharmaceutically acceptable salt thereof.

75. A method according to claim 62 wherein the somatostatin agonist is

$$HO(CH_2)_2$$
 — N — CH_2 -CO-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂.

or a pharmaceutically acceptable salt thereof.



30

35

- -4976. A method according to claim 62 wherein the somatostatin agonist is D-Phe-cyclo(Cys-Phe-D-Trp-Lys-Thr-
- 77. A method according to claim 2 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 1 than the other human somatostatin sub-type receptors.

Cys) -Thr-al or a pharmaceutically acceptable salt thereof.

- 78. A method according to claim 2 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 2 than the other human somatostatin sub-type receptors.
- 79. A method according to claim 2 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 3 than the other human somatostatin sub-type receptors.
- 80. A method according to claim 2 wherein the somatostatin agonist has a higher binding affinity for human somatostatin sub-type receptor 4 than the other human somatostatin sub-type receptors.
- 81. A method according to claim 2 wherein the somatostatin agonist has a nigher binding affinity for human somatostatin sub-type receptor 5 than the other human somatostatin sub-type receptors.
- 82. A method according to claim 2 wherein the

 25 somatostatin agonist has a higher binding affinity for two or

 more of human somatostatin receptor sub-types 1, 2, 3, 4

 and/or 5.
 - 83. A method according to claim 2 wherein the somatostatin agonist is

$$R_1$$
 $A^1-A^2-A^3-D-Trp-Lys-A^6-A^7-A^6-R_3$

10

15

20

Phe, p-X-Ane, or o-X-Phe;

 A^2 is Ala, Leu, Ile, Val, Nie, Phe, β -Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe; A^3 is pyridyl-Ala, Trp, Phe, β -Nal, 2,4-dichloro-Phe, pentafluoro-Phe o-X-Phe, or p-X-Phe;

A⁶ is Val, Ala, Leu, Ile, Nle, Thr, Abu, or Ser;
A⁷ is Ala, Leu, Ile, Val, Nle, Phe, β-Nal, pyridyl-Ala,
Trp, 2,4-dichloro-Phe, pentafluoro-Phe, c-X-Phe, cr p-X-Phe;
A⁸ is a D- or L isomer cf Ala, Leu, Ile, Val, Nle, Thr,
Ser, Phe, β-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe,
pentafluoro-Phe, p-X-Phe, or c-X-Phe;

wherein X for each occurrence is independently selected from the group consisting of $2N_3$, Cl, Br, F, OH, OCH₃ and NO₂; each R₁ and R₂, independently, is H, lower acyl or lower alkyl; and R₃ is OH or NH₂ provided that at least one of A¹ and A⁸ and one of A² and A⁷ must be an aromatic amino acid; and further provided that A¹ A², A⁷ and A⁸ cannot all be aromatic amino acids.

84. A method according to claim 2 wherein the somatostatin agonist is

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Thr-Phe-Thr-NH₂;

H-D-Phe-p-NO₂-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

H-D-Nal-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

H-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH₂;

H-D-Phe-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂;

H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂; or

H-D-Phe-Ala-Tyr-D-Trp-Lys-Val-Ala-β-D-Nal-NH₂ or a pharmaceutically acceptable salt thereof.

85. A method according to claim 2 wherein the somatostatin agonist is

```
D-Phe-CVs-Phe-D-Trp-Lys-Thr-Cys-\beta-Nal-NH<sub>2</sub>;
     D-Phe-Cyξ-Tyr-D-Trp-Lys-Thr-Cys-β-Nal-NH<sub>2</sub>;
     D-\beta-Nal-C/s-Phe-D-Trp-Lys-Thr-Cys-Thr-NH<sub>2</sub>;
     D-Phe-Cys-tyr-D-Trp-Lys-Thr-Pen-Thr-NH2;
     D-Phe-Cys-PAe-D-Trp-Lys-Thr-Pen-Thr-NH2;
     D-Phe-Cys-Ty\ -D-Trp-Lys-Thr-Pen-Thr-OH;
     D-Phe-Cys-Phe\D-Trp-Lys-Thr-Pen-Thr-OH;
     Gly-Pen-Phe-D-Arp-Lys-Thr-Cys-Thr-OH;
     Phe-Pen-Tyr-D-Tap-Lys-Thr-Cys-Thr-OH;
     Phe-Pen-Phe-D-Tra-Lys-Thr-Pen-Thr-OH;
10
     H-D-Phe-Cys-Phe-D\Trp-Lys-Thr-Cys-Thr-ol;
     H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH2;
     H-D-Trp-Cys-Tyr-D-T/tp-Lys-Val-Cys-Thr-NH2;
     H-D-Trp-Cys-Phe-D-Trb-Lys-Thr-Cys-Thr-NH2;
     H-D-Phe-Cys-Tyr-D-Trp\tys-Val-Cys-Thr-NH2;
     H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Trp-NH2;
     H-D-Phe-Cys-Tyr-D-Trp-L\s-Vah-Cys-Thr-NH2;
     Ac-D-Phe-Lys -Tyr-D-Trp-Lys-Val-Asp-Thr-NH2, wherein an amide
     bridge is between Lys and Asp;
     Ac-hArg(Et)2-Gly-Cys-Ph -DT#-Lys-Thr-Cys-Thr-NH2;
20
      Ac-D-hArg(Et)<sub>2</sub>-Gly-Cys-Phe-V-Trp-Lys-Thr-Cys-Thr-NH<sub>2</sub>;
      Ac-D-hArg(Bu)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH2;
      Ac-D-hArg(Et)2-Cys-Phe+D-Tr#-Lys-Thr-Cys-Thr-NH2;
      Ac-L-hArg(Et)2-Cys-Phe-Q-Drg-Dys-Thr-Cys-Thr-NH2;
      Ac-D-hArg(CH<sub>2</sub>CF<sub>3</sub>)<sub>2</sub>-Cys-Phe-D-Trh-Lys-Thr-Cys-Thr-NH<sub>2</sub>;
 25
      Ac-D-hArg(CH<sub>2</sub>CF<sub>3</sub>)<sub>2</sub>-Gly-Cys-Phe-D+Trp-Lys-Thr-Cys-Thr-NH<sub>2</sub>;
      Ac-D-hArg(CH<sub>2</sub>CF<sub>3</sub>)<sub>2</sub>-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH<sub>2</sub>;
      Ac-D-hArg(CH<sub>2</sub>CF<sub>3</sub>)<sub>2</sub>-Gly-Cys-Phe-D-1/rp-Lys-Thr-Cys-Thr-NHEt;
      Ac-L-hArg(CH<sub>2</sub>-CF<sub>3</sub>)<sub>2</sub>-Gly-Cys-Phe-D-trp-Lys-Thr-Cys-Thr-NH<sub>2</sub>;
      Ac-D-hArg(CH<sub>2</sub>CF<sub>3</sub>)<sub>2</sub>-Gly-Cys-Phe-D-Try-Lys(Me)-Thr-Cys-Thr-NH<sub>2</sub>;
 30
      Ac-D-hArg(CH<sub>2</sub>CF<sub>3</sub>)<sub>2</sub>-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NHEt;
       Ac-hArg(CH3, hexyl)-Gly-Cys-Phe-D-Tro-Lys-Thr-Cys-Thr-NH2;
       H-hArg(hexyl)2-Gly-Cys-Phe-D-Trp-Lys (Thr-Cys-Thr-NH2;
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Ad-D-hArg(Et)<sub>2</sub>-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHEt;
    Ac-Q-hArg(Et)<sub>2</sub>-Gly-Cys-Phe-D-Trp-Lvs-Thr-Cys-Phe-NH<sub>2</sub>;
    Proplonyl-D-hArg(Et)2-Gly-Cys-Phe-D-Trp-Lvs(iPr)-Thr-Cvs-Thr-
    NH<sub>2</sub>;
    Ac-D-β-Nal-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Gly-hArg(Et)2-NH2;
    Ac-D-Lys (12r) -Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH2;
    Ac-D-hArg(Ch2CF3)2-D-hArg(CH2CF3)2-Gly-Cys-Phe-D-Trp-Lys-Thr-
    Cys-Thr-NH2;
    Ac-D-hArg(CH<sub>2</sub>CF)<sub>2</sub>-D-hArg(CH<sub>2</sub>CF<sub>2</sub>)<sub>2</sub>-Gly-Cys-Phe-D-Trp-Lys-Thr-
10
    Cys-Phe-NH<sub>2</sub>;
    Ac-D-hArg(Et)2-D-hArg(Et)2-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-
    Ac-Cys-Lys-Asn-4-Cl-Ahe-Phe-D-Trp-Lys-Thr-Phe-Thr-Ser-D-Cys-
    NH2;
    Bmp-Tyr-D-Trp-Lvs-Val-C
15
     Bmp-Tyr-D-Trp-Lys-Val-Cys-PMe-NH2;
     Bmp-Tyr-D-Trp-Lys-Val-Cys-X+Cl-Phe-NH2;
     Bmp-Tyr-D-Trp-Lys-Val (Cys-) Nal-NH2;
     H-D-β-Nal-Cys-Tyr-D-Tro-Lys-Val-Cys-Thr-NH2;
    H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH2;
20
     H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cy\-β-Nal-NH<sub>2</sub>;
     H-pentafluoro-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH2;
     Ac-D-β-Nal-Cys-pentafluoro-Phe-D-Trh-Lys-Val-Cys-Thr-NH<sub>2</sub>;
     H-D-\beta-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-\beta-Nal-NH_2;
    H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-\beta-Na\lambda-NH_2;
25
     H-D-β-Nal-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH<sub>2</sub>;
     H-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Tht-NH2;
     Ac-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Tha-NH2;
     H-D-Phe-Cys-β-Nal-D-Trp-Lys-Val-Cys-Thr-NH<sub>2</sub>;
    H-D-Phe-Cys-Tyr-D-Trp-Lys-Cys-Thr-NH2;
     cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe);
     cyclo (Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe);
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cvclo (Pro-Phe-D-Trp-Lys-Thr-N-Me-Phe);
    cyclo (N-Me-Ala-Tyr-D-Trp-Lys-Thr-Phe);
    cyclo (Pro-Tyr-D-Trp-Lys-Thr-Phe);
    cycla (Pro-Phe-D-Trp-Lys-Thr-Phe);
    cyclo\(Pro-Phe-L-Trp-Lys-Thr-Phe);
    cyclo (Pro-Phe-D-Trp(F)-Lys-Thr-Phe);
    cyclo (Pko-Phe-Trp(F)-Lys-Thr-Phe);
    cyclo (Prd-Phe-D-Trp-Lys-Ser-Phe);
    cyclo (Pro-Phe-D-Trp-Lvs-Thr-p-C1-Phe);
    cyclo (D-Ala\N-Me-D-Phe-D-Thr-D-Lys-Trp-D-Phe);
    cyclo (D-Ala-M-Me-D-Phe-D-Val-Lys-D-Trp-D-Phe);
    cyclo (D-Ala-N-Me-D-Phe-D-Thr-Lys-D-Trp-D-Phe);
    cyclo (D-Abu-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Tyr);
    cyclo (Pro-Tyr-D-Arp-t-4-AchxAla-Thr-Phe);
    cyclo (Pro-Phe-D-TAp-t-A-AchxAla-Thr-Phe);
    cyclo (N-Me-Ala-Tyr-V
                              -Lys-Val-Phe);
    cyclo (N-Me-Ala-Tyr-PATrp-#-4-AchxAla-Thr-Phe);
    cyclo (Pro-Tyr-D-Trp-4 Amphe-Thr-Phe);
    cyclo (Pro-Phe-D-Trb-4-Ambhe-Thr-Phe);
    cyclo (N-Me-Ala-Tyr-D-Trp 4-Amphe-Thr-Phe);
20
    cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
    cyclo (Asn-Phe-Phe-D-Trp-Ly&-Thr-Phe-Gaba-Gaba);
    cyclo (Asn-Phe-D-Trp-Lys-Thr-Phe);
    cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-NH(CH2)4CO);
    cyclo (Asn-Phe-Phe-D-Trp-Lys-Th\-Phe-β-Ala);
25
    cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr\Phe-D-Glu) -OH;
    cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe);
    cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-GAy);
    cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba);
    cyclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gly);
30
    cyclo (Asn-Phe-Phe-D-Trp(F)-Lys-Thr-Phe-Gaba);
    cyclo (Asn-Phe-Phe-D-Trp(NO<sub>2</sub>)-Lys-Thr-Phe-Gaba);
    cvclo (Asn-Phe-Phe-Trp(Br)-Lys-Thr-Phe-Gaba);
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Ayclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Phe(I)-Gaba);
   cvclo (Asn-Phe-Phe-D-Trp-Lys-Thr-Tyr(But)-Gaba);
   cyclo (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys) -OH;
   cycld (Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys) -OH;
   cyclo\(Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Tpo-Cys)-OH;
   cyclo Amp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-MeLeu-Cys) -
   OH;
    cyclo (Phe-Phe-D-Trp-Lys-Thr-Phe-Phe-Gaba);
    cyclc (Phe Phe-D-Trp-Lys-Thr-Phe-D-Phe-Gaba);
    cyclo (Phe-Ahe-D-Trp(5F)-Lys-Thr-Phe-Phe-Gaba);
    cyclo (Asn-Phe-Phe-D-Trp-Lys(Ac)-Thr-Phe-NH-(CH2)3-CO);
    cyclo (Lys-Phe-D-Trp-Lys-Thr-Phe-Gaba);
    cyclo (Lys-Phe-the-D-Trp-Lys-Thr-Phe-Gaba); or
    cyclo (Orn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba) or a
    pharmaceutically acceptable salt thereof.
         86. A method according to claim 2 wherein the
    somatestatin agonist\sum \beta-\beta-Nal-Cys-Tyr-D-Trp-Lys-Thr-Cys-
    Thr-NH2 or a pharmace tidally acceptable salt thereof.
                A method according to claim 2 wherein the
    somatostatin agonist is -Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-
20
    NH2 or a pharmaceutically acceptable salt thereof.
          88. A method according to claim 2 wherein the
    somatostatin agonist is
                       \stackrel{\hat{}}{N} — (CH_2)_2-SO\stackrel{\hat{}}{A}D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH_2,
or a pharmaceutically acceptable salt thereof.
          89. A method according to t laim 2 wherein the
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somatostatin agonist is

$$HO(CH_2)_2 - N$$
 $N - CH_2-CO-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH2,$



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- of a pharmaceutically acceptable sait thereof.
- 90. A method according to claim 2 wherein the some ostatin agonist is D-Phe-cyclo(Cys-Phe-D-Trp-Lys-Thr-Cys)-Thr-ol or a pharmaceutically acceptable salt thereof.
- 9). A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is in the kidney.
- 92. A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is in the lung.
- 93. A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is in the liver.
 - 94. A method according to claim 57 wherein the fibrosis induced by a drag or a combination of drugs is in the skin.
 - 95. A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is of the central nervous system.
 - 96. A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is in bone or bone marrow.
- 97. A method according to claim 57 wherein the fibrosis of induced by a drug or a combination of drugs is in the cardiovascular system.
 - 98. A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is in an endocrine organ.
 - 99. A method according to claim 57 wherein the fibrosis induced by a drug or a combination of drugs is in the gastrointestinal system.
 - 100. A method according to claim 59 wherein the fibrosis induced by a disease state is in the idney.
 - 101. A method according to claim 38 wherein the fibrosis induced by a disease state is in the lung.
 - 102. A method according to claim 58 wherein the fibrosis induced by a disease state is in the liver



- $N_{
 m 403}.$ A method according to claim 58 wherein the fibrosis induced by a disease state is in the skin.
- 104\ A method according to claim 58 wherein the fibrosis induced by a disease state is of the central nervous system.
- 105. A method according to claim 58 wherein the fibrosis induced by a disease state is in bone or bone marrow.
 - 106. A method according to claim 58 wherein the fibrosis induced by a $d_{\mathbf{t}}^{\mathbf{t}}$ sease state is in the cardiovascular system.
- 107. A method according to claim 58 wherein the fibrosis induced by a distase state is in an endocrine organ. 10
 - 108. A method according to claim 58 wherein the fibrosis induced by a disease state is in the gastrointestinal system.
- 109. A method according to claim 59 wherein the fibrosis induced by an environmental or an industrial factor is in the 15 kidney.
 - 110. A method accdrdipg to claim 59 wherein the fibrosis induced by an environmental or an industrial factor is in the lung.
- 111. A method according to claim 59 wherein the fibrosis induced by an environmental or an industrial factor is in the 20 liver.
 - 112. A method according to claim 59 wherein the fibrosis induced by an environmental or \setminus an industrial factor is in the skin.
- 113. A method according to diaim 59 wherein the fibrosis 25 induced by an environmental or an industrial factor is of the central nervous system.
- 114. A method according to claim 59 wherein the fibrosis induced by an environmental or an industrial factor is in bone or bone marrow. 30
 - 115. A method according to claim 59\wherein the fibrosis induced by an environmental or an industrial factor is in the cardiovascular system.





- \$\psi 16. A method according to claim 59 wherein the fibrosis induced by an environmental or an industrial factor is in an endocrine organ.
- 117. A method according to claim 59 wherein the fibrosis induced by an environmental or an industrial factor is in the gastrointestinal system.
 - 118. A method according to claim 60 wherein the fibrosis induced by an immune reaction is in the kidney.
- 119. A method according to claim 60 wherein the fibrosis 10 induced by an immune reaction is in the lung.
 - 120. A method according to claim 60 wherein the fibrosis induced by an immune reaction is in the liver.
 - 121. A method according to claim 60 wherein the fibrosis induced by an immune reaction is in the skin.
- 122. A method according to claim 60 wherein the fibrosis 15 induced by an immune readtion is of the central nervous system.
 - 123. A method according to $\frac{1}{2}$ to wherein the fibrosis induced by an immune reaction is in bone or bone marrow.
- 124. A method according the claim 60 wherein the fibrosis 20 induced by an immune reaction is in the cardiovascular system.
 - 125. A method according to claim 60 wherein the fibrosis induced by an immune reaction $i \not\models in$ an endocrine organ.
 - 126. A method according to claim 60 wherein the fibrosis induced by an immune reaction is in the gastrointestinal system.
 - 127. A method according to claim 2 wherein the fibrosis is induced by a wound.
 - 128. A method according to claim 127 wherein the fibrosis induced by a wound is in the kidney.
 - 129. A method according to claim 127 wherein the fibrosis induced by a wound is in the lung.



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- 130. A method according to claim 127 wherein the fibrosis induced by a wound is in the liver.
- 131 A method according to claim 127 wherein the fibrosis induced by a wound is in the skin.
- 132. A method according to claim 127 wherein the fibrosis induced by a wound is of the central nervous system.
- 133. A method according to claim 127 wherein the fibrosis induced by a wound is in bone or bone marrow.
- 134. A method according to claim 127 wherein the 10 fibrosis induced by a wound is in the cardiovascular system.
 - 135. A method according to claim 127 wherein the fibrosis induced by a wound is in an endocrine organ.
 - 136. A method according to claim 127 wherein the fibrosis induced by a wound is in the gastrointestinal system.
 - 137. A pharmaceutical composition useful for inhibiting fibrosis in a patient which comprises a pharmaceutically acceptable carrier and an effective amount of somatostatin, somatostatin agonist or a pharmaceutically acceptable salt thereof.
 - 138. A pharmaceutical composition according to claim
 137 wherein the composition comprises a somatostatin agonist
 or a pharmaceutically acceptable salt thereof.
- 139. A pharmaceutical composition useful for inhibiting overexpression of TGF-β which comprises a pharmaceutically acceptable carrier and an effective amount of somatostatin, somatostatin agonist or a pharmaceutically acceptable salt thereof.
- 140. A pharmaceutical composition according to claim 139
 30 wherein the composition comprises a somatostatin agonist or a pharmaceutically acceptable salt thereof.
 - 141. A method of claim 2, wherein said somatostatin agonist is administered orally.

